REMARKS/ARGUMENTS

1. Objections to the Specification

The disclosure of the was objected to because of the incorrect recitation of US Serial Number 08/107, 908. The specification has been corrected by amendment to recite US Patent Nos. 6, 168, 942, 6, 410,032 and 6, 410, 299 all of which claim the benefit of US Application Serial No. 60/107,908.

2. Claim Objections

Claim 13 was objected to because it ended in two periods. Claim 13 has been canceled.

3. Claim Rejections –35 U.S.C § 112 ¶ 2

Claims 1-4 were rejected as allegedly being indefinite for recitation of the word "5' region"

Claims 2,3,5,6,7 were rejected as allegedly being indefinite for recitation of "degenerate variants".

Claims 6 was rejected as allegedly being indefinite for the use of the word "essentially".

Claims 13 and 15 were rejected as allegedly being indefinite for "reciting a mutation into the 3' region of the N^{pro} protease gene"

Claim 14 was rejected as allegedly being indefinite for reciting "about" one third of the N^{pro} protease gene"

In order to facilitate prosecution Applicants have presented new claims but reserve the option to represent the originally filed claims in a related application. Applicants believe the current claims comply with all aspects of **35 U.S.C § 112 ¶ 2**

4. Claim Rejections –35 U.S.C § 112 ¶ 1 ---Written Description

Claims 2,3,5-7, 9-12 and 16-19 were rejected as allegedly failing to comply with the written description requirement for reciting "degenerative variants". In order to facilitate prosecution applicants have presented new claims which make it clear that a "degenerate variant" is one which encodes the same amino acid sequence.

5. Claim Rejections –35 U.S.C § 112 ¶ 1 ---Enablement

(a) Claim 8 is rejected as allegedly not being enabled. The Examiner has indicated that claims reciting "ATCC NO: PTA-2532" are allegedly not enabled. Applicant's attorney submits with this paper a statement that the deposit is made under the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposit on the availability will be

irrevocably removed upon the granting of the patent.

(b) Claims 1-7 and 9-29 were also rejected as allegedly lacking enablement for failure to recite "where in the genome the mutation is". Applicants reserve the right to present the original claims in a related application but herewith present new claims to facilitate prosecution.

The Examiner also states that there is:

> "no indication or data presented that would indicate that the present viruses are sufficiently attenuated to ameliorate or prevent viral infection".

The Examiner cites *Tautz* for this proposition but *Tautz* is inapplicable as it deals with a ubiquitin insertion in an entirely different area of the genome. The specification makes it clear that the region to be mutated is the 3' end of the N^{pro} protease gene. US Patent Nos. 6, 168, 942, 6, 410,032 and 6, 410, 299, all of which are incorporated by reference, make it abundantly clear that a mutated N^{pro} protease gene does result in an attenutated phenotype.

(c) Claims 13 and 15 were rejected as drawn to a method of modifying wild type BVDV by introducing a mutation into the 3' region that renders the N^{pro} region inactive. The Examiner asserts that the mutation is required to be singular and that therefore this means it must a mutation "affecting a single nucleotide" The specification defines mutation at paragraph [0034} of the published application however, and makes it clear that "mutation" include substitutions, deletions, and insertions of one or more base pairs.

The Examiner states:

> The specification does not teach or provide a working example of a single mutation that could be made to the N^{pro} gene that render the resulting protein inactive.

Applicants would point out that they have indeed identified the area to be mutated and point it out with particularity in the claims by specifying that the 5' proximate region must remain intact. In addition, US Patent Nos. 6, 168, 942, 6, 410,032 and 6, 410, 299 (incorporated by reference) make it clear that one of ordinary skill when faced with the problem of inactivating N^{pro} is quite able to predict and screen mutations which are likely to result in an inactive gene.(see particularly US Patent 6,186,942). Applicants would point out that they have specified a only a small area of the genome to be mutated and have modified the claim with a functional limitation. Functional limitations are specifically authorized in sequence claims by the Revised Written Description Guidelines at Example 14. Applicants would also point out in light of the

enabling disclosure of , US Patent Nos. 6, 168, 942, 6, 410,032 and 6, 410, 299 that they are not required to specifically point out each and every nucleotide to be modified to obtain an inactive N^{pro} gene. The Applicants would point the Examiner to *In re Angstad*, 190 USPQ 214, (C.C.P.A. 1976)

> We cannot agree with the board that appellants' disclosure is not sufficient to enable one of ordinary skill in the art to practice the invention without undue experimentation. .... The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples or the disclosure of "thousands" of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed.

The question is not, as noted in *Angstad*, whether Applicant's have tested each and every embodiment of their invention covered by a claim but whether they have enabled one of ordinary skill to make and use their invention. Applicant's assert unequivocally that they have.

6. Claim Rejections ---35 USC 102(b)

The Examiner alleges that the GenEmbl database accession number AF039181 anticipates claim 8 which recites ATCC No. PTA-2532 or SEQ ID NO:12. SEQ ID NO:12 is disclosed as a sequence which is 16, 758 nucleotides in length. AF039181 discloses a sequence which is annotated as being "BVDVNADL 5' untranslated region" and which is 385 nucleotides of sequence identical to SEQ ID NO:12.

An anticipatory reference must disclose each and every element of the claimed invention either implicitly or explicitly. Applicants would respectfully submit that AF039181 and *Topliff et al.*

simply do not disclose their invention. and would request the rejection be withdrawn as to all claims.

Respectfully submitted,

Edward P. Rehberg

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Edward P. Rehberg, Attorney
Registration No. 34,703
Pfizer, Inc.
Patent Department
301 Henrietta Street
KZO-32-LAW
Kalamazoo, Michigan 49007
Telephone No. (269) 833-7829 or (269) 833-9500
Telefax No. (269) 833-8897 or (269) 833-2316